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Patient-reported barriers and facilitators to antiretroviral adherence in sub-Saharan Africa

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Objective: The aim of this study was to identify the range and frequency of patient-reported barriers and facilitators to antiretroviral treatment (ART) adherence in sub-Saharan Africa (SSA).

Design: Studies from 2005 to 2016 were identified by searching 10 electronic databases and through additional hand and web-searching.

Methods: Inclusion criteria were HIV-positive adults taking ART based in any SSA country, qualitative study or quantitative survey and included at least one patient-reported barrier or facilitator to ART adherence. Exclusion criteria were only including data from treatment-naïve patients initiating ART, only single-dose treatment, participants residing outside of SSA and reviews.

Results: After screening 11 283 records, 154 studies (161 papers) were included in this review. Forty-three barriers and 30 facilitators were reported across 24 SSA countries. The most frequently identified barriers across studies were forgetting ($n=76$), lack of access to adequate food ($n=72$), stigma and discrimination ($n=68$), side effects ($n=67$) and being outside the house or travelling ($n=60$). The most frequently identified facilitators across studies were social support ($n=60$), reminders ($n=55$), feeling better or healthier after taking ART ($n=35$), disclosing their HIV status ($n=26$) and having a good relationship with a health provider ($n=22$).

Conclusion: This review addresses the gap in knowledge by collating all the patient-reported barriers and facilitators to ART adherence in SSA. Current barriers measures need to be adapted or new tools developed to include the wide variety of factors identified. The factors that have the greatest impact need to be isolated so interventions are developed that reduce the barriers and enhance the facilitators.

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Keywords: Africa South of the Sahara, AIDS, antiretroviral therapy, HIV, medication adherence

Introduction

Nearly 25 million people, 70% of all those living with HIV globally, live in countries in sub-Saharan Africa (SSA) [1]. HIV is a debilitating disease; however,

antiretroviral treatment (ART) helps promote effective viral suppression, reduces the risk of transmission and prevents death [2,3]. To ensure positive treatment outcomes, high levels of ART adherence (80–95%) are necessary depending on the regime potency [4–6];

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however, a meta-analysis [7] indicated that 23% of Africans were achieving less than 80% adherence, potentially impacting on prognosis.

Mills *et al.* [3] conducted a systematic review in 2005 of patient-reported barriers and facilitators to ART adherence globally. This review identified important barriers, in both high-income countries (HIC) and low and middle-income countries (LMIC), which included substance abuse, forgetfulness, pill burden, fear of disclosure, falling asleep, decreased quality of life, access to medication, being suspicious of the treatment, work and family responsibilities and complicated regimens; however, only 12 (14.3%) of the studies included were conducted in LMIC of which only five were in SSA. ART availability in SSA has improved since this review was conducted, with 1.3 million patients receiving ART treatment in 2006; a 10-fold increase on patients with access 3 years earlier [8]. The lack of treatment availability would have impacted the number of studies being conducted in this region, which has steadily increased over the past decade.

No facilitators were identified by Mills *et al.* in LMIC [3]; however, important facilitators were identified, including seeing positive effects of medication, accepting their HIV status, using reminders, having a simple regimen, sense of self-worth and understanding the need for strict adherence. Although some similarities were found between different settings and countries, the review urged the need to determine the patient-important factors for adherence in LMIC [3] due to the number of people living with HIV in these areas and the unique psycho-socio-political environments.

In the past decade, there has been a shift in simply identifying and reporting rates of nonadherence and an increased focus on identifying and addressing barriers and facilitators to ART adherence in LMIC, in particular in SSA [9–11]; therefore, this systematic review is a critical update. The review identifies adult patient-reported barriers and facilitators to ART adherence in SSA from 2005 to 2016 in studies with qualitative and quantitative methodology.

Materials and methods

Search strategy

The review was conducted in-line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA) [12]. N.C. performed searches on 10 databases on 24 May 2016: Cochrane Library, MEDLINE (OVID), PsycINFO (OVID), PsycARTICLES (OVID), EMBASE (OVID), Global Health (OVID), CINAHL (EBSCO), International Bibliography of the Social Science (IBSS; Proquest),

Applied Social Sciences Index and Abstracts (AIDIA; Proquest) and African Index Medicus (AIM; WHO). Search terms were varied to adapt to the different requirements of the different databases. The search included terms related to HIV, ART, SSA countries and adherence (see supplementary material for full example of search strategy, <http://links.lww.com/QAD/B44>).

All databases were searched from 2005 to 24 May 2016 to investigate the research published since the review by Mills *et al.* [3]. All records were downloaded into ENDNOTE (X7.4).

Hand-searching, web-searching and forward citation searching were conducted to find other relevant published and unpublished studies. Abstracts from the following international conferences were searched: International AIDS Society (IAS; 2005–2015), Conference on Retroviruses and Opportunistic Infections (CROI; 2014, 2016), AIDS Impact (2009–2015) and International AIDS Conference (2006–2014). For all potentially relevant abstracts, if no published article was found, the authors were contacted for more details if possible. Reference lists of included articles and systematic reviews were searched. Searches in Google Scholar were conducted using search terms such as ‘adherence’, ‘HIV’ and ‘Sub-Saharan Africa’. Forward tracking of the review by Mills *et al.* [3] was also performed in the Web of Science database.

Study selection

N.C. reviewed all the titles and abstracts of each record to assess potential relevance and M.Ah. examined a random sample (10%) and a concordance rate was measured. Acceptable concordance was predefined as agreement on at least 90%, which is the same as other health reviews [13,14]. N.C. reviewed the full text for any potentially relevant studies to assess eligibility. Eligible studies met the following criteria: based in SSA, original research, any language, qualitative study or quantitative survey and included an adult patient-reported barrier or facilitator to ART adherence. Studies were excluded if they only focused on initiation to ART in treatment-naïve participants, only utilized a single dose of ART treatment, for example prophylaxis, only focused on Africans living in a non-SSA country or were only reviews.

Quality assessment

N.C. completed quality assessment for all included studies. M.Ah. assessed a random sample of 30 (15 qualitative and 15 quantitative). The RATS (Relevance, Appropriateness, Transparency, Soundness) measure [15] was used to assess the qualitative studies and a measure developed by Hawker *et al.* [16] was used to assess the quantitative studies (see supplementary material for further details, <http://links.lww.com/QAD/B44>).

Data extraction

N.C. extracted all the data into a predesigned Excel spreadsheet that was double checked for accuracy. After an initial read of all qualitative papers, a list of all key barriers and facilitators were identified and were combined into themes. N.C., L.D.H. and M.Ab. discussed the themes and any disputes were resolved (see supplementary material for further details on extraction, <http://links.lww.com/QAD/B44>). Due to

the considerable heterogeneity of the studies, a meta-analysis was not suitable.

Results

A total of 161 papers involving 154 studies were identified for inclusion. The search of the 10 databases provided a total of 11 283 citations (see Fig. 1). After adjusting for

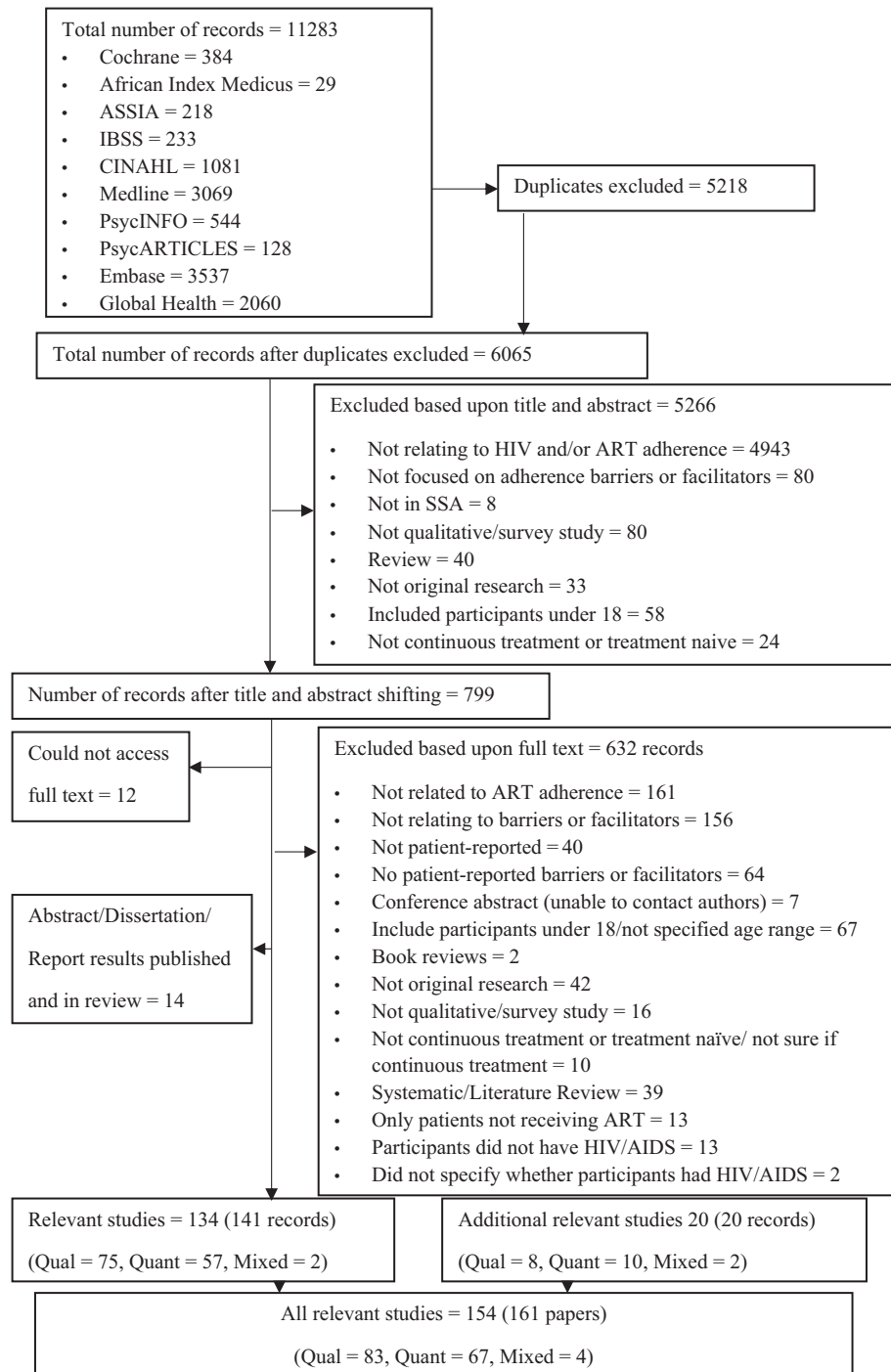


Fig. 1. Flowchart.

duplicates, 6065 citations remained. Of these, 5266 citations were excluded after reviewing the title and abstracts. The majority of these were excluded (4943; 93.9%) because they were not related to HIV or adherence. The remaining 323 citations (6.1%) were excluded based upon other criteria.

The full text of the remaining 799 potentially relevant citations were searched for; however, 12 (1.5%) could not be retrieved. The full texts of the remaining 787 papers were examined in more detail. Fourteen were excluded (1.8%) because the search had identified both published and unpublished formats of the same studies; therefore, the published versions were retained. A further 632 papers (80.3%) were excluded based upon inclusion and exclusion criteria. From the 141 relevant papers (17.9%) identified, 134 relevant studies were included. From the additional searching, a further 20 studies were identified that met the criteria for inclusion. An acceptable concordance of 91.0% was achieved between N.C. and M.Ah. for inclusion of studies.

Overall, 154 studies were eligible of which 83 were qualitative [17–99], 67 were quantitative [100–166] and four were mixed [167–170], which included at least one patient-reported barrier or facilitator in both the qualitative and quantitative studies included in the paper. Three studies were published in French [116,137,149] and a fluent French speaker was utilized to extract the data and translate into English. The remaining studies were published in English.

Description of studies

A total of 37 175 HIV-positive participants were included across all 154 quantitative and qualitative studies of which 36 476 were prescribed ART. Within the 87 qualitative studies, 3247 HIV-positive participants were included of whom 2824 were prescribed ART. Within the 71 quantitative studies, 33 928 HIV-positive participants were included of whom 33 652 were prescribed ART (see supplementary material (Table 3) for a description of each study, <http://links.lww.com/QAD/B44>).

Studies were conducted in 24 countries in SSA with six studies including more than one country [45,64,84,95, 124,130]. More than half the studies (59.7%) were conducted across South Africa, Uganda, Ethiopia and Kenya.

Just over half of the qualitative studies conducted semi-structured in-depth interviews (IDIs) (49; 56.3%) [17,20–22,26,27,29,32–37,39–43,45–47,49,51,54–60, 62,63,65–67,69–71,78,81,84,85,87–90,95–97,165] with their HIV-positive participants. Eighteen studies (20.7%) used focus group discussions (FDGs) [19,23–25,28,50, 53,61,68,73,74,76,77,82,94,98,167,169], 16 used both IDIs and FDGs (18.4%) [18,30,31,38,44,52,64,72,75,79, 83,86,92,93,99,170], one used free attitude interviews

(FAIs) and FDGs (1.1%) [80], one used group sessions without more detail [168], one used IDIs and life history and illness narratives [48] and one used digital stories [91].

The majority of the quantitative surveys (54; 76.1%) were administered by an interviewer [100,102,104–109, 112,113,115–117,119,121–124,128–130,133–137,139, 141–150,152–166,168,169], five (7.0%) were self-administered [125,126,132,140,151], one (1.4%) used an audio computer-assisted self-interview [110] and the remaining studies (11; 15.5%) did not specify or it was not clear how the survey was administered [101,103,111,114, 118,120,127,131,138,167,170]. No studies indicated clearly that there was a free response option for participants to report the barriers they experienced (for further description on the studies see the supplementary material, <http://links.lww.com/QAD/B44>).

Quality assessment

The qualitative studies showed overall high quality, with 98.9% of studies including all RATS items related to relevance of study question, 72.4% including the item related to appropriateness of qualitative method and 83.5% including all items related to soundness of interpretive approach, with the exception of poor transparency of the procedure (only 55.0% of studies included all items). In particular, studies required more information regarding recruitment (only 23.0% of studies included this), who chose not to participate and why (only 20.7% included this), end of data collection justification (25.0% included this) and researcher bias (16.1% included this). The quantitative studies showed overall fair/good quality (9.2% of studies being assessed as good across categories and 65.9% being assessed as fair), with the exception of the ethics and bias category (49.3% assessed as poor and 12.7% assessed as very poor). Only 5.6% of studies were assessed as good quality in this category, which required papers to include explicit details regarding issues of patient confidentiality, sensitivity and informed consent. Researchers also were required to be reflexive or be aware of any potential bias they may have. One-third of studies (32.4%) acknowledged these issues without including explicit details; however, the majority either briefly mentioned them or did not include them (see supplementary material for further details, <http://links.lww.com/QAD/B44>).

Barriers

Forty-three unique patient-reported barriers were identified in 79 (90.8%) of the qualitative and 68 (95.8%) of the quantitative studies that we developed into nine themes comprising financial constraints, problems with their health provider and other interpersonal relationships, issues regarding medication collection and medication taking, treatment-related challenges, problems with their mental health and well-being and beliefs about HIV and treatment as well as specific beliefs about ART. See Table 1 for a list of the themes and both

Table 1. Barriers and facilitators.

Themes	Barriers (<i>n</i> of studies that reported factor)	Facilitators (<i>n</i> of studies that reported factor)
Financial	Lack of money for transport to ART clinic (32) Lack of money for HIV care (19) Do not want to lose disability grant (6) ^d	Grant or livelihood support (5) ^d Free ART treatment (4)
Health provider	Dissatisfaction with HIV/ART information provided (17) Experienced negative treatment from clinic staff (10) Unable to gain attention from staff (9) Poor relationship with health provider (5) ^d	Good relationship with health provider (22) ^d Receiving counselling and/or teaching (17)
Medication taking	Forgetting (76) ^a Lack of access to adequate food (72) ^{b,d} Stigma and discrimination (68) Outside house or travelling (60) ^c Being busy (30) Run out of ART (26) Sleeping (22) Difficulty taking ART in private (17) ^a Change in daily routine (15) No access to liquids (6) ^{a,d}	Reminders (55) Having a routine (9) ART packaging (7) Access to food and/or water (6) ^d Carrying ART whilst out of the house (5)
Interpersonal relationships	Lack of social support (22) ^d Sharing or selling ART (7) HIV nondisclosure (21) ^d Sex (wives have lack of autonomy) (6)	Social support (60) ^{a,d} Having disclosed HIV status (26) ^d Want to live and take care of children (21) Attending a support group (11) Seeing others improve on ART (6) Want to look healthy to others (5) Staying away from negative relationships (2) Feeling better or healthier (35) ^f Being able to work again (13) ‘Normalization’ – feeling the same as others or same as before HIV (8) Fewer HIV/AIDS-related illnesses (8) Prayers or faith in God (8) Being hopeful (6) ^d Want to take control of their health (13) Improved knowledge and understanding of HIV/ART (10) Accept own HIV status (7) ^d
Mental health and well being	Feeling sick or ill (30) ^d Using alcohol or other substances (27) ^a Feeling better or healthier (26) ^e Low mood or stress (22) ^a Feeling hopeless (7) ^d Feeling lonely (4)	Feeling better or healthier (35) ^f Being able to work again (13) ‘Normalization’ – feeling the same as others or same as before HIV (8) Fewer HIV/AIDS-related illnesses (8) Prayers or faith in God (8) Being hopeful (6) ^d Want to take control of their health (13) Improved knowledge and understanding of HIV/ART (10) Accept own HIV status (7) ^d
Beliefs about HIV and treatment	Religious beliefs or treatments (27) ^a Traditional beliefs or medicines (20)	Want to take control of their health (13) Improved knowledge and understanding of HIV/ART (10) Accept own HIV status (7) ^d
Beliefs about ART	Fear of cause of HIV (6) Denial of HIV status (4) ^d Negative attitude towards treatment regime (19) ART will not work (7) ^d ART is harmful (7) Lack of motivation to take ART (7) Should not mix ART with other treatments (4)	Belief in ART benefit (20) ^d Do not want to be ill again (14) Adherence self-efficacy (8) ART helps you look healthy to others (5) God provided ART (4)
Medication collection	Erratic clinic drug supply (22) Long clinic waiting times (13) ^a Long distance to the clinic (8) Unable to get to clinic due to work constraints (7)	
Treatment-related factors	Side effects (67) ^c Pill burden (20) Problem with physical characteristics of Pills (4)	

ART, antiretroviral treatment.

^aOne mixed-methods study identified the barriers or facilitators in both the qualitative and quantitative components.^bThree mixed-methods studies identified the barriers or facilitators in both the qualitative and quantitative components.^cTwo mixed-methods studies identified the barriers or facilitators in both the qualitative and quantitative components.^dComparable barriers and facilitators across themes.^eSame factor as both a barrier and facilitator.^fSame factor as well as a comparable factor to another barrier or facilitator.

the barriers and facilitators included within each theme (see supplementary material, <http://links.lww.com/QAD/B44> for further details including a list of studies that reported each factor as well as the frequency of nonadherent participants within each study that reported each barrier or facilitator if reported).

Facilitators

Thirty patient-reported facilitators were identified in 76 (87.4%) of the qualitative and 21 (29.6%) of the quantitative studies. Seventeen facilitators (56.7%) were only identified in the qualitative studies. The facilitators are composed of seven of the same themes as the barriers

excluding medication collection and treatment-related factors (see Table 1). Due to the comparable themes, the barriers and facilitators will be described together.

Themes

There were several factors that impacted adherence related to finance as well as each patient's health provider. Within the finance theme, in particular not receiving financial help was a barrier, whereas receiving funds was a benefit. Across studies, the fifth most reported facilitator was having a good relationship with their health provider ($n=22$). The opposite was identified as a barrier, however, only by a few studies ($n=5$).

Four of the five most-reported barriers across all studies were classified into the medication-taking theme; forgetting ($n=76$), lack of access to adequate food ($n=72$), stigma and discrimination ($n=68$) and being outside the house or travelling ($n=60$). Some of these had comparable facilitators, including having reminders to take medication [which was the second most reported facilitator ($n=55$)], having access to food or water and carrying ART whilst out of the house, although the latter two were only identified by a small number of studies.

Interpersonal relationships included the first and fourth most reported facilitators [social support ($n=60$) and having disclosed their HIV status ($n=26$)]. Both of these included comparable barriers (e.g. lack of social support and HIV nondisclosure) indicating that an absence of these factors is a barrier to adherence.

Mental health and well-being was the only theme to include the same factor as both a barrier and facilitator, feeling better or healthier after ART treatment. This factor was the third most reported facilitator across studies ($n=35$), although 26 studies also reported it as a barrier. Another comparable barrier to feeling better was also reported (feeling sick or ill) indicating that the opposite can also hinder adherence. Feeling hopeless and being hopeful were both reported as comparable factors, although only reported in a few studies.

The patients' beliefs about HIV and treatments theme also included factors that acted as a barrier or facilitator. Both religious and traditional beliefs and treatments were indicated as a barrier to adhering to ART, whilst a patient's desire to take control of their health was a facilitator. Denial of one's own HIV status was reported as a barrier and had a comparable facilitator of accepting one's own HIV status, although these were reported by a small number of studies. Specific beliefs about ART also showed to have an impact on adherence. The belief in the benefit of ART was reported ($n=20$) as a facilitator, whereas believing ART will not work was reported as a barrier, but only by seven studies in comparison.

Both medication collection and treatment-related factors only included barriers. The latter theme included the fourth most reported barrier across studies, side effects ($n=67$). Erratic clinic drug supply and long waiting times were reported by the most studies as a barrier to ART adherence in the medication collection theme.

Discussion

Summary of evidence

In this systematic review, a total of 43 patient-reported barriers and 30 facilitators to ART adherence were identified in 154 studies across 24 SSA countries. Barriers and facilitators to ART adherence included factors related to participants' physically taking their ART medication (e.g. unable to take their pills without adequate food or using reminders to remember to take their pills), factors that impacted participants' physical or mental health (e.g. feeling sick or feeling better after taking ART), factors related to participants' relationships with other people (e.g. nondisclosure of HIV status to others or social support), factors related to finance (e.g. lack of money for HIV care or free ART treatment), factors related to participants' health provider including all staff (e.g. experiencing negative treatment from clinic staff or having a good relationship with their health provider), beliefs around HIV and treatments for HIV (e.g. using traditional medicines or accepting own HIV status) and beliefs regarding ART (e.g. ART is harmful or ART is beneficial). Factors related to collecting medication at the clinic (e.g. long waiting times or erratic drug supply) and treatment-related factors (e.g. side effects or pill burden) were only reported as barriers to ART adherence. One factor was both a barrier and facilitator (e.g. feeling better after taking ART), which emphasizes medication-adhering behaviour is not universal and it is necessary to explore this individually. The most frequently identified barriers across studies and methodologies were forgetting, lack of access to adequate food, stigma and discrimination, side effects and being outside the house or travelling. The most frequently identified facilitators across studies and methods were social support, using reminders, feeling better or healthier after taking ART, disclosing their HIV status and having a good relationship with a health provider. This review helps identify the range and frequency of factors that impact ART adherence for patients within a variety of different settings in SSA.

Other systematic reviews have focused on specific types of adherence barriers, including geographic and transport-related barriers in SSA [171], food insecurity [172] and depression and alcohol use in SSA [173]. These reviews are useful because they go in-depth into one type of barrier and they may focus on HIV outcomes other than adherence [171]; however, this review is necessary to

give an overview of the many factors that affect ART adherence in SSA.

Frequency across studies does not necessarily equate with importance for individuals; therefore, the most reported factors may not have the greatest impact upon adherence. Unfortunately, the low number of studies that included the nonadherent within-study frequencies means it is difficult to compare the impact of these on adherence. Future studies should include these to allow researchers to ascertain not only the range of factors that affect adherence but also the impact of each.

This review identified 26 barriers that were not previously reported in SSA in the previous systematic review [3], including traditional medicines, religious beliefs or treatments, lack of access to food and sharing medication. These need to be acknowledged when working with people living with HIV in SSA. The five most frequently reported facilitators were included in the previous review [3], showing that there is similarity between patients in HIC and LMIC; however, several others were identified that had not been previously noted, for example financial aid, access to food and water and religious beliefs. This further confirms that there are factors that may be more applicable to LMIC that therefore need particular consideration when designing interventions to improve ART adherence.

Understanding and being aware of these are important for policy makers, researchers and health professionals. Although patients denied missing ART doses to their health professional, if a barrier measure was used, patients would then reveal nonadherence by indicating the barriers that prevent them from adhering [174]. Having a list of barriers that are applicable to the context is essential. There are some differences between HIC and LMIC and this should be reflected in the provisions available for patients. Although general and HIV-specific measures for barriers to adherence do currently exist [175–179], none encompass the wide range of reasons identified in this review. Developing or adapting a measure that can be utilized by health professionals in SSA is necessary. In particular, the most commonly used self-report HIV adherence measure [180] (Adult AIDS Care Trials Group [AACTG]) includes a ‘reasons for non-adherence’ subscale [175] that needs to be adapted if used in SSA to include all relevant factors. To our knowledge, there is not a similar measure for facilitators and research needs to explore whether assessing the facilitators may be equally as helpful as the barriers to reach the level of desired adherence.

Immediate treatment initiation after diagnosis has been shown to have more positive HIV outcomes than later [181,182] and thus may become the recommended start date globally. There are debates in the literature about the practicalities associated with immediate ART initiation

[183], including increased burden on the healthcare system, increased frequency of risk behaviours when receiving ART and ethical issues such as resource allocation in low-resource settings [183]. The impact of certain barriers may increase, such as the factors associated with healthcare; therefore, the need to enhance the facilitators will become greater.

Future research needs to help identify the barriers and facilitators that have the greatest impact on adherence and help develop interventions based upon these. Within SSA, there have been several interventions focused on helping participants remember their medication, whereas less have focused on lack of food or stigma [184]. Research needs to explore whether these other interventions would have a greater influence on adherence. In addition, the focus on adherence interventions in SSA has often been observational and more randomized control trials (RCTs) are required [184].

Limitations

Although efforts were made to include all eligible studies, it is possible that not all studies exploring barriers and facilitators to ART adherence in SSA were included, as research from resource-constrained settings may be less likely to be published or not indexed in the major databases [185]. The studies are not easily compared due to the heterogeneity of how factors and adherence were measured. There was a great variety of within-study frequency measurement; therefore, only studies that included the frequency of reporting within nonadherent participants were included. Also, some studies combined separate factors into one, so it was not possible to extract the individual factors. The quality of the studies seemed generally fair; however, there were areas of poor quality. As two measures were utilized in quality assessment, it is not easy to compare the quality across both qualitative and quantitative studies.

The majority of the qualitative studies identified both barriers and facilitators, whereas the majority of the quantitative studies only identified barriers. This bias may have prevented certain facilitators from being identified. Barrier measures or adapted versions [175,177,186–189] were utilized in some surveys that may have caused certain barriers to be reported more frequently; however, other important barriers may have been missed because they were not included.

Conclusion

This review highlights the range and frequency of barriers and facilitators that affect ART adherence in HIV adult patients in SSA. Research needs to help identify which factors have the greatest impact on adherence and develop interventions accordingly. Measures need to be developed or adapted for SSA to include all the relevant factors. Interventions need to be developed that aim to reduce the barriers and enhance the facilitators. By understanding

and being able to identify what hurdles a patient experiences and how certain aspects may encourage them to adhere, the focus is now on using this information to help patients achieve optimum ART outcomes.

Acknowledgements

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Conflicts of interest

There are no conflicts of interest.

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